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Case Report

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Priapism a rare side effect of cilostazol

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ABSTRACT

We present the case of priapism associated with cilostazol. A rare side effect of cilostazol on the genitourinary system. Priapism is a long-lasting erection that occurs without sexual arousal or stimulation. It can cause irreversible damage on penis. Therefore, urgent treatment is required. Priapism can be treated with aspiration, intracavernous injection or, as in our case, with surgical ligation.Priapism is a common side effect of phosphodiesterase 5 inhibitors. However, this situation is very rare for cilostazol, one of the phosphodiesterase 3 inhibitors.

Keywords: Phosphodiesterase 3 inhibitor, priapism, leukocytosis, thrombocytosis, aspiration

INTRODUCTION

Priapism is a prolonged erection of penis. It is an unwanted, painful erection of the penis that lasts more than four hours and is unrelated to sexual desire.[1] It occurs when there is a problem with the blood flow to penis, and this can be caused by blood diseases, penis injury, certain medications, penile cancer and alcohol or drug use.[2] Drug-induced priapism comprises about 30% of cases. The drugs most frequently implicated are psychotropic drugs (phenothiazines and trazodone), antihypertensives (mainly prazosin) and heparin. Recently, the intracavernosal injection of vasoactive drugs (papaverine and phentolamine) has been described in patients treated for impotence. With the exception of heparin, an alpha-adrenergic blocking mechanism has been suggested in the priapism-inducing action of these drugs. A significant number of anecdotal case reports link priapism and drugs, and it is possible that certain cases of idiopathic priapism could be reclassified if accurate pharmacological anamnesis were to be performed.[3]

To our knowledge, this case is about priapism, one of the very rare side effects of cilostazol.

Cilostazol is a quinolone derivative primarily used to treat intermittent claudication due to peripheral vascular disease. Cilostazol is also indicated for secondary prevention in patients with a history of transient ischemic attacks or non-cardioembolic ischaemic stroke. Cilostazol improves walking distance by promoting vasodilation and antiplatelet activity with inhibition of phosphodiesterase III and subsequent increases in available cAMP.[4]

Common side effects of cilostazol are chest pain, pounding heartbeats, fever, chills, sore throat, mouth sores; or easy bruising, unusual bleeding.[5] Additionally, there are few reports of cilostazol induced nephrotoxicity.[6,7]

However, priapism is not one of the common known effects of cilostazol. This side effect of the drug is very rare and we have not come across any reported cases.

Priapism must be considered an urological emergency. Surgical procedures are the most preferred treatment for this condition but, in selected cases, drug treatment seems to be an alternative approach.[3]

CASE

In August 2024, a 75-year-old male patient with a history of angiography, bypass benign prostatic hyperplasia, and hypertension came to the emergency room with a complaint of priapism. The patient had a complaint of priapism and dysuria that had been ongoing for 2 days. He was using the following drugs: clopidogrel, lasix, spironolactone, trazodone, carvedilol, pitavastatin, acetylsalicylic acid. The patient also stated that he started taking a drug called cilastazol 10 days ago. His physical examination was normal. His blood pressure was 135/73, His body tempature was 36,7°C, and his heart rhythym was 75 beats per minute.

As seen in the Table blood sample results were normal except for thrombocytosis and leukocytosis.

The patient was consulted to urology and hematology deparments. The patient had no history of using any additional medication other than cilostazol in the last month. Therefore the use of the drug cilostozol was discontinued. Leukocytosis and thrombocytosis were seen as side effects of the drug,

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Table. Blood tests throughout patient hospital stay

Blood tests	Day 1	Day 2	Day 3
wbc	16.2 K/µL	17.8 K/µL	17.6 K/µL
neu	10.9 K/µL	13.8 K/µL	13.08 K/µL
hb	11.4 g/dl	9.2 g/dl	9.2 g/dl
plt	12.1 K/µL	1177 K/µL	1002 K/µL

however, hematology called the patient for a later clinic check-up for detailed investigation.

A focused urology exam reviewed an erected penis with evidence of ischemia. Therefore, it was decided to perform aspiration.

Aspiration was performed by the urologist from the roots of the corpus cavernosum. Patient's priapism persisted despite aspiration and the procedure was interrupted because the patient exhibited hypotensive symptoms such as cold sweat and blurred vision during the procedure. The patient was treated with 1000 ml of normal saline solution as an IV bolus. When the patient's vital signs returned to the normal range, the patient was monitored and the aspiration procedure was continued. The aspiration process took almost 3 hours. A large amount of blood was discharged from the glans penis. The hemogram value decreased by 2 units, but the penis still did not become completely flaccid. Therefore the patient was scheduled for surgery and admitted to the urology service.

After the operation, the patient's penis became flaccid and the patient was subsequently discharged on the following day.

DISCUSSION

Drugs that generally cause priapism are phosphodiesterase type 5 (PDE5) inhibitor. PDE5 inhibitors, including sildenafil and tadalafil, are widely used for the treatment of erectile dysfunction, pulmonary arterial hypertension, and certain urological disorders. This group of drugs causes the blood vessels in the penis to dilate, increasing blood flow and facilitating erections.[8]

Prazosin is an alpha blocker and increases the risk of priapism by dilating blood vessels. However, this risk is quite low.

Heparin is an anticoagulant and in rare cases increases the risk of priapism by changing blood flow.

Phenothiazines increase the risk of priapism when taken in high doses due to their effects such as dopamine blockade.

As a result, the drugs with the highest risk of priapism are phenothiazines, followed by PDE5 inhibitor. Prazosin and heparin carry a lower risk.

But in our case the drug that caused the side effect was cilostazol. Cilostazol, like another anticoagulant drug such as heparin, may cause priapism.

Cilostazol; primarily used in the treatment of intermittent claudication, is a 2-oxyquinolone derivative that works through the inhibition of phosphodiesterase III and related increases in cyclic adenosine monophosphate (cAMP) levels. However, cilostazol has been implicated in a number of other basic pathways including the inhibition of adenosine reuptake, the inhibition of multidrug resistance protein 4, among others. It has been observed to exhibit antiplatelet, antiproliferative, vasodilatory, and ischemic-reperfusion protective properties (Figure). As such, cilostazol has been investigated for clinical use in a variety of settings including intermittent claudication, as an adjunctive for reduction of restenosis after coronary and peripheral endovascular interventions, and in the prevention of secondary stroke.[2]

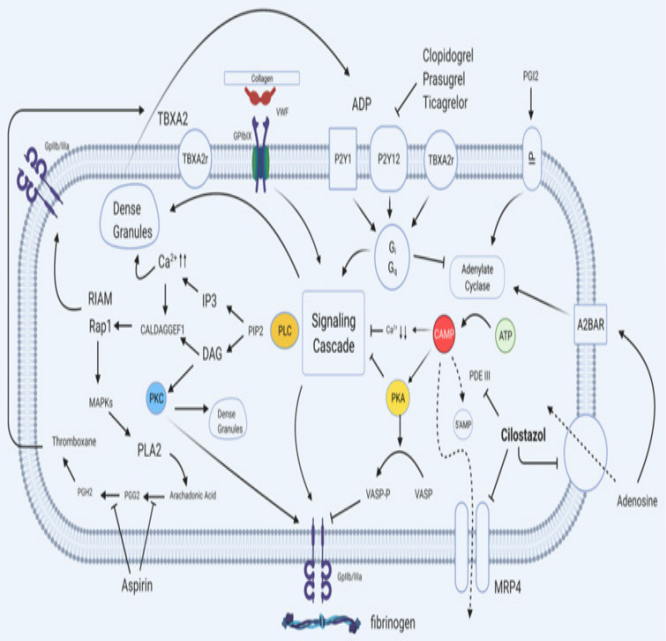

Figure. Illustration of platelet activation signaling cascade and the impact of cilostazol[7]

In our case, the patient had started using cilostazol approximately 10 days ago due to claudication.

A common complaint is intermittent claudication, characterised by pain in the legs or buttocks that occurs with exercise and which subsides with rest. Cilostazol has been shown to be of benefit in improving walking distance in people with intermittent claudication secondary to peripheral arterial disease.[9]

Cilostazol is a generally well-tolerated oral medication. The most common side effects of cilostazol are headache, diarrhea, and palpitations.[10]

Also It can induce tachycardia, tachyarrhythmia, and hypotension, thrombocytopenia or leukopenia.[11,12] Also rarely can cause nephrotoxicity.[6,7]

This case shows us that cilostazol causes erectile dysfunction even though it is a phosphodiesterase 3 inhibitor.

Cilostazol may increase the risk of priapism under 4 conditions:

1-Personal health problems, especially issues related to vascular health and blood flow.
2-Genetic and biological factors can affect a person's susceptibility to side effects from medications.
3-Combining it with medications that affect blood and blood flow may increase the risk of priapism.
4-High doses and long-term use of the drug is also one of the factors that increase the risk.

CONCLUSION

Based on our case, we may draw the conclusion that, cilostazol may cause priapism. When we disgusted with the cardiovascular surgery department, he said that such cases were rare but an expected side effect. Therefore, before starting

treatment, side effects should be considered. Patients should be informed about possible side effects.

Priapism requires immediate treatment and can cause permanent damage to penis if left untreated. If it lasts longer than 36 hours, scarring and permanent erectile dysfunction will likely occur. Therefore emergency treatment should be applied to patients developing priapism. We may rarely encounter such cases in the emergency department, which is why we wanted to present this case to you.

ETHICAL DECLARATIONS

Informed Consent
The patient signed and free and informed consent form.

Referee Evaluation Process
Externally peer-reviewed.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Financial Disclosure
The authors declared that this study has received no financial support.

Author Contributions
All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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